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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/579,780	05/18/2006	Yoshiya Oda	042715-5019	5776

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EXAMINER	
GAKH, YELENA G	

ART UNIT	PAPER NUMBER
1797	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/579,780	ODA ET AL.	
	Examiner	Art Unit	
	Yelena G. Gakh, Ph.D.	1797	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 June 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-117* is/are pending in the application.

4a) Of the above claim(s) *21-24 and 27-117* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-20,25 and 26* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Election of claims 1-20 and 25-26 without traverse filed on 06/26/09 is acknowledged. Claims 1-117 are pending in the application. Claims 21-24 and 27-117 are withdrawn from consideration.

Double Patenting

2. Applicant is advised that should claims 1, 2 or 6 be found allowable, claim 25 will be objected to under 37 CFR 1.75 as being a substantial duplicate thereof. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k). The claim is repeating the subject matter of claims 1, 2 or 6.

Claim Rejections - 35 USC § 112

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 1-20 and 25-26 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the method for which the biological molecule is a known molecule, does not reasonably provide enablement for the method, in which the biological molecule is not known. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims. There is no way to add an internal standard, prepared from the metabolically isotope labeled biological molecule, if this molecule is not known.

Claims 1-3, 5-6, 8-10, 13-20 and 25-26 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabled for the internal standard, in which the biological molecule is present in the known quantity, does not reasonably provide enablement for the internal standard, in which the quantity of the biological molecule is not known. There is no way for a person of ordinary skill in the art to use the internal standard as quantification standard, if

the biological molecule, which is used for such quantification, is not present in the standard in the known quantity.

5. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claims 1-20 and 25-26 rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1, 3-4, 6-7, 9-11 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: obtaining metabolically isotope labeled biological molecule. This step is essential to the method, since otherwise it is totally unclear, as to where from the biological molecule is obtained to be metabolically isotope labeled, which renders the method recited in the claims unclear to the practitioner in the art.

Claim 11 is unclear. What does it recite? Quantitating a biological molecule in the internal standard, which is a metabolically labeled biological molecule? This does not make any sense.

Claim 12 is totally unclear. First, it is unclear, as to what might be "the step according to claim 11". Which step is meant here? What is a "non-isotope labeled synthetic peptide"? How is it labeled? Is it related anyhow to the biological molecule?

However, the most unclear is the step of extracting and fractionating a biological molecule from the internal standard substance that is the metabolically isotope labeled biological molecule.

In fact, claims 11 and 12 are so unclear that the examiner is not able to perform a thorough search on the claims, since it is not apparent, as to which steps are recited in the claimed method.

From claim 14 it is not apparent, as to what does it mean that the sample is unable to be labeled by a cell culture? Why should it be labeled by the cell culture?

From claim 15 it is totally unapparent, as to how a biological molecule can be a combination of different biological molecules recited in the claim?

Claims 25 and 26 provide for the use of an internal standard and a cell, but, since the claims do not set forth any steps involved in the method/process, it is unclear what method/process applicant is intending to encompass. A claim is indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practiced.

Claims 25 and 26 are rejected under 35 U.S.C. 101 because the claimed recitation of a use, without setting forth any steps involved in the process, results in an improper definition of a process, i.e., results in a claim which is not a proper process claim under 35 U.S.C. 101. See for example *Ex parte Dunki*, 153 USPQ 678 (Bd.App. 1967) and *Clinical Products, Ltd.* v. *Brenner*, 255 F. Supp. 131, 149 USPQ 475 (D.D.C. 1966).

Furthermore, all claims recite an indefinite article "a" in front of the "biological sample". Does it mean that in each claim a biological sample is different from the one recited in the parent claim?

Claim Rejections - 35 USC § 102

7. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

8. **Claims 1-10 and 13-19** are rejected under 35 U.S.C. 102(a) as being anticipated by Wu et al. (Anal. Chem., 2004, July 23) (Wu).

Wu teaches a method for quantitating a biological molecule in a sample with a mass spectrometer, comprising adding to the sample an internal standard substance that is a metabolically isotope labeled biological molecule (see Abstract). "We have developed a method to metabolically label mammalian organisms with ^{15}N to produce tissue-specific internal standards for global quantitative proteomic analyses of tissues. A labeling period of 44 days in a male rat resulted in a mean ^{15}N atomic enrichment of >90% in liver and plasma. These rat tissues provided an optimal source of tissue-specific internal standards to facilitate the quantitative proteomic analyses of complex mammalian tissue samples. Subsequent quantitative shotgun comparisons of rat liver lysates prepared from cycloheximide-treated and untreated animals using the ^{15}N liver standards reveal novel insight into global cellular responses to the reduction

of protein synthesis using sublethal doses of the drug, cycloheximide." (Pages 4951-4952) (*Claims 1, 3-10, 15-16, 18-19*).

After the standard was added, the proteins were extracted, fractionated, digested and analyzed on mass spectrometer (pages 4952 and 4953) with quantification of proteins by determining a ratio of intensities between labeled and unlabeled peaks of each molecule (page 4955) (*Claims 2 and 17*). The samples were cells extracted from tissues (*Claims 13 and 14*).

Claim Rejections - 35 USC § 103

9. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

10. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

11. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

12. **Claim 20** is rejected under 35 U.S.C. 103(a) as being unpatentable over Wu. While Wu utilizes ^{15}N labeling of the sample, ^{13}C labeling is a well known modification for isotope

enrichment of the biological molecules for performing mass spectrometry analysis, and therefore it would have been obvious for a routineer in the art to use ^{13}C-labled samples instead of ^{15}N labeled samples as taught by Wu.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Yelena G. Gakh, Ph.D. whose telephone number is (571) 272-1257. The examiner can normally be reached on 9:30 am - 6:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Vickie Y. Kim can be reached on (571) 272-0579. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Yelena G. Gakh/
Primary Examiner, Art Unit 1797

8/31/2009